

Amendments to the Specification

Please replace the paragraph beginning on page 186, line 1 with the following amended paragraph:

FIGS. 83 and 84 depict other shapes for openings that may be used to define the size, but not the shape, of a cavity that is formed in a silicon substrate. As can be seen in these examples, the size of the cavity is determined by the length and width of the openings. For example, in FIG. 83A, two slots are depicted. The width of the first slot and the width of the second slot control the size of the etching but, to some extent, allow a pyramidal cavity to be formed. Other shapes, as depicted in the other figures, may be used to form cavities. Generally, ~~the~~ to form a cavity having a predefined shape, an opening, need only have a width and length that corresponds to the length and width of the desired cavity regardless of the shape of the opening.

Please replace the paragraphs beginning on page 186, line 25 with the following amended paragraphs:

FIGS 84 A-C depict alternate embodiments of masks having openings that produce projections after etching. As depicted in these figures different size shapes may produce different size cavities. As described in more detail below, the ability to form different size cavities and different having masks with different size openings may be useful for placing particles in the cavities. Any of the cavities formed with the above described mask may be formed through substrate ~~Error! Reference source not found.~~ such that a bottom opening is also present.

An integrated cover layer of flexible projections 1340 formed in mask ~~Error! Reference source not found.~~ 1320 may provide a method of retaining particle 1350 in cavity ~~Error! Reference source not found.~~ 1330. In an embodiment shown in FIG. 85, flexible projections 1340 may be produced over cavity 1330. Mask opening ~~Error! Reference source not~~

~~found.1310~~ may be smaller than the top of underlying cavity ~~Error! Reference source not found.1330~~. Particle 1350 may be inserted through flexible projections 1340 into cavity ~~Error! Reference source not found.1330~~ as depicted in FIG. 85. As particle 1350 passes flexible projections 1340, the flexible projections may elastically bend downward, as shown in FIG. 85B and FIG. 85C, until the particle passes completely by the flexible projections and into cavity ~~Error! Reference source not found.1330~~. As shown in FIG. 85D, after particle 1350 passes flexible projections 1340, the flexible projections may elastically return to their original position, thereby providing retention of the particle in cavity ~~Error! Reference source not found.1330~~. Retention of particle 1350 in cavity ~~Error! Reference source not found.1330~~ may be maintained by flexible projections 1340 during subsequent handling of the sensor array.

FIG. 86 shows cross sectional and top views of cavity ~~Error! Reference source not found.1330~~ with flexible projections 1340 formed for specific size selection of particle 1350 to be captured and retained in the cavity. In one embodiment, a 100 cm² silicon substrate may have from about 10¹ to about 10⁶ mask openings and cavities. Mask openings ~~Error! Reference source not found.1310~~ may be substantially the same size across substrate ~~Error! Reference source not found.1300~~, or may be of different sizes. As shown in FIG. 86, the size and shape of top opening 1360 of cavity ~~Error! Reference source not found.1330~~ may be determined by location of corners 1380 of opening ~~Error! Reference source not found.1310~~ in mask ~~Error! Reference source not found.1320~~. Size and shape of bottom opening 1370 may be determined by location of corners 1380 and thickness of substrate ~~Error! Reference source not found.1300~~. As such, the size and shape of the top and bottom openings for each cavity may be controlled independently. Each cavity ~~Error! Reference source not found.1330~~ and flexible projections 1340 may be designed for a specific size particle 1350.

An array of cavities ~~Error! Reference source not found.1330~~ in substrate ~~Error! Reference source not found.1300~~ may be formed to automatically sort specific size particles 1350 into specific cavities based on a size of the particle; e.g., based on the diameter of the particle. Large particle 1350 with a diameter larger than top opening 1360 of cavity ~~Error!~~

~~Reference source not found.1330~~ may be substantially inhibited from entering the cavity. Large particle 1350 with a diameter smaller than bottom opening 1370 of cavity ~~Error!~~
~~Reference source not found.1330~~ may enter top opening 1360 through flexible projections 1340. Smaller particle 1350 will then pass through bottom opening 1370 and out of the cavity. Small particle 1350 with a diameter smaller than top opening 1360 and larger than bottom opening 1370 may be captured in cavity ~~Error!~~ ~~Reference source not found.1330~~ and retained in the cavity with flexible projections 1340.

In an embodiment of a sensor array, different sized particles 1350 may be used to target different types of analytes of interest. A mixture of particles having predetermined sizes may be introduced to the array. The array of cavities ~~Error!~~ ~~Reference source not found.1330~~ may be designed for specific particle sizes to automatically sort the correct size particle 1350 into each cavity. In a sensor array system, flexible projections 1340 may be transparent to the wavelength of light of a light source used for illuminating particles 1350 in cavities ~~Error!~~ ~~Reference source not found.1330~~.

In an embodiment, a particle may be placed in a cavity using various techniques. Micromanipulators may be used in for individual placement of a particle in a cavity or particles in an array of cavities. A vacuum or flow system may be used for more rapid placement of particles in an array of cavities. In an embodiment, a substrate may be fabricated a cavity or cavities designed to select a desired particle size. A solution with a wide particle size distribution range may be produced. The substrate may be dipped into the solution. A vacuum or other fluid flow may pull a particle past flexible projections and into a top opening of a cavity. A too large particle may not pass through the top opening into the cavity. A too small particle may pass through the cavity and out a bottom opening of the cavity. The flexible projections may not necessary bend as a particle passes through the projections if the particle is too large. A particle of desired size may pass through the flexible projections and the top opening and be retained in the cavity.

In another embodiment, a cavity is formed in a substrate by undercutting a mask to produce flexible projections in the mask during anisotropic etching of a silicon substrate as described previously. The integrated cover layer formed by the mask and flexible projections and the top and bottom opening of the cavity in the substrate may be fabricated for a desired diameter size of a particle in a shrunken state. A particle to be placed within the cavity may be exposed to a medium in which the particle may be caused to shrink. As shown in FIG. 87A, particle 1350 may be easily inserted through flexible projections 1340 into cavity **Error!** ~~Reference source not found.1330~~ of substrate **Error!** ~~Reference source not found.1300~~ in its shrunken state. After insertion of particle 1350 into cavity **Error!** ~~Reference source not found.1330~~, the particle may be exposed to a medium which causes the particle to return to its normal state as shown in FIG. 87B. Particle 1350 may be captured within cavity **Error!** ~~Reference source not found.1330~~ by flexible projections 1340 after it returns to its normal size. By correctly designing the swollen state of particle 1350 and flexible projections 1340, the particle may be retained within the cavity during subsequent processing.